IN THE UNITED STATES DISTRICT COURT FOR THE
EASTERN DISTRICT OF VIRGINIA
Alexandria Division

THE CLEVELAND CLINIC FOUNDATION, et al.,	)	
Plaintiffs	)	
v.	)	1:17-cv-198 (LMB/IDD)
TRUE HEALTH DIAGNOSTICS, LLC,	)	
Defendant.	)	

MEMORANDUM OPINION

Plaintiffs The Cleveland Clinic Foundation ("CCF") and Cleveland Heartlab, Inc. ("CH") (collectively, "plaintiffs"), have filed a three-count complaint for patent infringement against defendant True Health Diagnostics, LCC ("True Health" or "defendant"), alleging that the defendant's procedures for diagnosing atherosclerotic cardiovascular disease ("CVD")[1] infringe three patents owned by the plaintiffs: U.S. Patent 9,575,065 ("the '065 patent") (Count 1); U.S. Patent 9,581,597 ("the '597 patent") (Count 2); and U.S. Patent 9,612,242 ("the '242 patent") (Count 3). Defendant moved to dismiss all three counts, arguing that the patents asserted in the first two counts are directed to an unpatentable natural law, and that plaintiffs did not adequately plead that defendants infringe the patent asserted in the third count. On June 9, 2017, the Court denied that motion without prejudice for two reasons. First, an appeal was still pending before the Federal Circuit in a related civil action in which the Northern District of Ohio held the parent patent of the '065, '597, and '242 patents to be invalid. As a matter of prudence and judicial

[1] According to the specification of the '065 patent, CVD "is the general term for heart and blood vessel diseases, including atherosclerosis, coronary heart disease, cerebrovascular disease, and peripheral vascular disease. Cardiovascular disorders are acute manifestations of CVD . . . . CVD accounts for one in every two deaths in the United States and is the number one killer disease." [Dkt. 35-1] at C0000318.

economy, it made sense to wait for the Federal Circuit's disposition rather than attempt to predict what it was going to do. Second, in the absence of a ruling from the Federal Circuit, the Court concluded that additional factual discovery would likely be necessary to determine whether certain steps claimed in the patents were conventional.

The Federal Circuit has now resolved that appeal, affirming the conclusion that the parent patent was invalid because it was directed toward subject matter that falls within a judicial exception to 35 U.S.C. § 101, which sets the outer limit of what is eligible for patent protection. Cleveland Clinic Found. v. True Health Diagnostics, LLC, 859 F.3d 1352 (2017) ("Cleveland Clinic I"). In light of that ruling, True Health has filed a motion to reconsider the decision as to Counts 1 and 2, arguing that the Federal Circuit's opinion renders additional factual discovery unnecessary and that those counts should now be dismissed.[2] For the reasons that follow, the Court is persuaded that the Federal Circuit's opinion in Cleveland Clinic I fully resolved all relevant factual issues as to Counts 1 and 2 and defendant's Motion to Reconsider will be granted.

I. BACKGROUND

A. The Patents at Issue

All three of the patents at issue in this civil action are children of the now-invalidated U.S. Patent 7,223,552 ("the '552 patent"), and all involve identifying the levels of a particular enzyme—myeloperoxidase ("MPO")—in the blood stream of a person suffering from atherosclerotic CVD. The '552 patent contains 23 total claims, most of which are minor variations on Claim 1, which describes:

[2] Because the Motion to Reconsider does not address Count 3, this Memorandum Opinion does not further discuss the '242 patent.

1. A method for characterizing the test subject's risk of having atherosclerotic cardiovascular disease, comprising:

determining levels of [MPO] activity, [MPO] mass, or both in a bodily sample from the test subject, said bodily sample being blood, serum, plasma, blood leukocytes selected from the group consisting of neutrophils and monocytes, or any combination thereof,

wherein elevated levels of MPO activity or MPO mass or both in the bodily sample of the test subject as compared to at least one predetermined value based on levels of MPO activity, MPO mass or both, respectively, in comparable bodily samples obtained from control subjects diagnosed as not having the disease indicates that the test subject is at risk of having atherosclerotic cardiovascular disease.

[Dkt. 38-2] at 52.

As for the patents in this civil action, the '065 patent recites one claim:

1. A method of detecting elevated MPO mass in a patient sample comprising:

a) obtaining a plasma sample from a human patient having atherosclerotic cardiovascular disease (CVD); and

b) detecting elevated MPO mass in said plasma sample, as compared to a control MPO mass level from the general population or apparently healthy subjects, by contacting said plasma sample with anti-MPO antibodies and detecting binding between MPO in said plasma sample and said anti-MPO antibodies.

[Dkt. 35-1] at C0000332.

The '597 patent recites two claims:

1. A method for identifying an elevated myeloperoxidase (MPO) concentration in a plasma sample from a human subject with atherosclerotic cardiovascular disease comprising:

a) contacting a sample with an anti-MPO antibody, wherein said sample is a plasma sample from a human subject having atherosclerotic cardiovascular disease;

b) spectrophotometrically detecting MPO levels in said plasma sample;

c) comparing said MPO levels in said plasma sample to a standard curve generated with known amounts of MPO to determine the MPO concentration in said sample; and

d) comparing said MPO concentration in said plasma sample from said human subject to a control MPO concentration from apparently healthy human subjects, and identifying said MPO concentration in said plasma sample from said human subject as being elevated compared to said control MPO concentration.

2. The method of claim 1, further comprising, prior to step a), centrifuging an anti-coagulated blood sample from said human subject to generate said plasma sample.

[Dkt. 35-2] at C0000659.

The specifications for both the '065 and '597 patents provide that the inventions "relate[] to a diagnostic test which can be used to determine whether an individual or test subject is at a lower risk or higher risk of developing or having cardiovascular disease than other individuals in a given population of human subjects." [Dkt. 35-1] at C0000318; [Dkt. 35-2] at C0000645. In the "Summary of the Invention" section, both specifications provide that the "present invention provides new diagnostic tests for characterizing an individual's risk of developing or having cardiovascular disease . . . . based on the discovery that patients with coronary artery disease (CAD) have significantly greater levels of leukocyte and blood [MPO] levels than patients without angiographically significant CAD." Id. Both specifications state that "[MPO] activity may be determined by any of a variety of standard methods known in the art. [Dkt. 35-1] at C0000321; [Dkt. 35-2] at C0000648.

B. Prosecution History of The '065 and '597 Patents

The patent examiner initially rejected the '065 patent on § 101 grounds, concluding that it was directed toward an unpatentable abstract idea. Plaintiffs successfully challenged that decision, citing Example 29 from the U.S. Patent and Trademark Office's ("USPTO") Subject Matter Eligibility Examples in the guidelines that the USTPO issues to its examiners. Second Amended Complaint ("SAC"), [Dkt. 23-1] at 33.

Example 29 provides seven hypothetical claims regarding a fictitious autoimmune disease causing a facial rash called "julitis," which the hypothetical inventors have discovered can be distinguished from rosacea by examining a patient for the presence of a protein known as

"JUL-1." [Dkt. 35-7] at 13. The first three of the seven exemplary claims given in Example 29 are sufficient to illustrate the reasoning urged by the plaintiffs and adopted by the USPTO in evaluating plaintiffs' patent applications:

> 1. A method of detecting JUL-1 in a patient, said method comprising:
> a. obtaining a plasma sample from a human patient; and
> b. detecting whether JUL-1 is present in the plasma sample by contacting the plasma sample with an anti-JUL-1 antibody and detecting binding between JUL-1 and the antibody.
>
> 2. A method of diagnosing julitis in a patient, said method comprising:
> a. obtaining a plasma sample from a human patient;
> b. detecting whether JUL-1 is present in the plasma sample by contacting the plasma sample with an anti-JUL-1 antibody and detecting binding between JUL-1 and the antibody; and
> c. diagnosing the patient with julitis when the presence of JUL-1 in the plasma sample is detected.
>
> 3. A method of diagnosing julitis in a patient, said method comprising:
> a. obtaining a plasma sample from a human patient;
> b. detecting whether JUL-1 is present in the plasma sample by contacting the plasma sample with a porcine anti-JUL-1 antibody and detecting binding between JUL-1 and the porcine antibody; and
> c. diagnosing the patient with julitis when the presence of JUL-1 in the plasma sample is detected.

Id. at 14–15. According to the USPTO guidance, the first and third claims are patentable, but the second is not. Id. at 15–17. The USPTO considers the first claim eligible because the "steps do not recite or describe any recognized exception" to § 101. Id. at 15. In other words, the USPTO believes that "analysis of the claim as a whole indicates that the claim is focused on a process of detecting whether JUL-1 is present in a plasma sample, and is not focused on the [nature-based] products per se." Id. Claim 2, on the other hand, "describes a correlation or relationship between the presence of JUL-1 in a patient's plasma and the presence of julitis in the patient" that is a "naturally occurring correlation," meaning it is directed to a natural law. Id. at 15–16. Because the additional steps set out "well-understood, routine, and conventional activity," Claim

2 is unpatentable. Id. at 16. Although Claim 3 is very similar to Claim 2, in this hypothetical universe "detecting JUL-1 using a porcine antibody is an unconventional step" that renders the claim eligible for patent protection. Id. at 17 (emphasis added). In other words, in the USPTO's fictitious scenario, porcine antibodies were not previously used to detect JUL-1. Therefore, the claim is directed at the new method rather than the JUL-1-roseacea correlation.

After the USPTO initially found the three patents at issue in this civil action to be ineligible, plaintiffs argued that their claims more closely resembled the patentable first example than the unpatentable second example because they only claimed a method for detecting MPO rather than a method for diagnosing CVD. In reversing the finding of unpatentability for the '065 patent, the examiner accepted plaintiffs' argument, writing:

> Applicant's argument with respect to eligibility of the claim under the current USPTO life science subject matter eligibility examples (i.e., [E]xample 29, [C]laim 1) at pp. 9-10 of the response is considered persuasive. The current claim does not recite or describe any recognized [judicial exception]; the claim only recites obtaining a plasma sample from a human patient having atherosclerotic CVD and detected elevated MPO mass in the sample using anti-MPO antibodies.

SAC, [Dkt. 23-1] ¶ 35 (emphasis omitted). As a result of this finding, the '065 patent was issued on February 21, 2017. [Dkt. 35-1] at 1.

The '597 patent was likewise initially rejected on § 101 grounds, but eventually allowed after plaintiffs challenged that decision. SAC, [Dkt. 23-1] ¶ 40. In reversing the finding of unpatentability, the USPTO once again cited Example 29, Claim 1, and further elaborated:

> While the claims are directed to an abstract idea which is comparing MPO concentration in a plasma sample to a control, the claims are found to amount to significantly more than the judicial exception because the steps of a) contacting a plasma sample from a human subject having artherosclerotic CVD with an anti-MPO antibody and , [sic] spectrophotometrically detecting MPO levels in said plasma sample were routinely and conventionally engaged by one of skill in the art at the time the invention was made. In other words, while detecting MPO with an antibody and spectrophotometrically detecting MPO levels was known, said

> detecting steps were not routinely or conventional [sic] used to detect MPO levels in plasma samples from human subjects having artherosclerotic CVD.

Id. ¶ 41 (emphasis omitted). In short, the USPTO concluded that the claims described a new and unconventional application for known techniques. See id. In the USPTO's judgment, that was sufficient to overcome the § 101 challenge, and the '597 patent was issued on February 28, 2017. [Dkt. 35-2] at 1.

C. Alleged Infringing Activity

According to the complaint, in July 2015 True Health acquired certain assets of a laboratory services company, Health Diagnostics Lab ("HDL"), in a bankruptcy sale. SAC, [Dkt. 23-1] ¶ 28. Before its bankruptcy, HDL had entered into a Laboratory Services Agreement with plaintiff CH in which CH provided MPO testing "services and reagents" to HDL. Id. ¶ 25. When True Health purchased HDL's assets, it expressly excluded the Laboratory Services Agreement from its bid, and the bankruptcy court approved this exclusion on September 16, 2015. Id. ¶ 28.[3]

Plaintiffs allege that since acquiring HDL's assets True Health has been "conducting MPO testing" using products from Diazyme Laboratories. Id. ¶ 52. In particular, True Health "obtains plasma samples from human patients having atherosclerotic [CVD]" and uses the Diazyme assay to detect "elevated MPO mass in" those plasma samples." Id. ¶¶ 53–54. Plaintiffs also allege that True Health provides "testing services to detect MPO . . . by actually testing bodily samples for the presence of . . . MPO," using an assay that "employs a mass spectrometer." Id. ¶¶ 66, 70.

[3] According to the complaint, the CEO of CH wrote a letter to True Health warning them that, in CH's view, "any sale of MPO testing without authorization from" CH would violate CH's patent rights. SAC, [Dkt. 23-1] ¶ 29.

D. The Ohio Litigation

This lawsuit is the plaintiffs' second effort to sue True Health for patent infringement related to its MPO patents. The first attempt, in the Northern District of Ohio, failed. See Cleveland Clinic Found. v. True Health Diagnostics, LLC, No. 1:15-cv-2331, 2016 WL 705244 (N.D. Ohio Feb. 23, 2016), aff'd Cleveland Clinic I, 859 F.3d 1352. In that case, plaintiffs asserted four patents against True Health, three of which (the '552 patent, the '286 patent, and the '581 patent) taught "a method of analyzing MPO biomarkers in a patient's blood sample to predict a patient's potential for CVD."[4] Id. at *1 (internal footnote omitted). The fourth patent ("the '260 patent") taught "a method for administering a lipid lowering agent based on elevated levels of MPO." Id.

In Cleveland Clinic I, the district court granted defendant's motion to dismiss all counts, holding that three of the four patents at issue, including the '552 patent, were directed to an unpatentable natural law—namely, the correlation between elevated MPO levels and CVD—and that the patents added no "inventive concept" to the natural law that elevated MPO levels accompany CVD, observing that "a myriad of methods well-known in the art existed at the time of invention."[5] 2016 WL 705244 at *5–*6. The Federal Circuit affirmed, rejecting plaintiffs' contention that the district court improperly treated certain claims in the challenged patents as representative and concluding that resolution of the § 101 issue was appropriate "before claim construction or significant discovery has commenced." Cleveland Clinic I, 589 F.3d at 1360. It then considered the patents in light of the two step framework introduced by Alice Corp. Pty.

[4] "The '552 patent [taught the method] with regard to a typical patient, while the '286 and the '581 patent[s] [were] directed at patients presenting with chest pain." Cleveland Clinic, 2016 WL 705244, at *1.

[5] The fourth count was dismissed because the court found that the complaint failed to adequately allege infringement.

Ltd. v. CLS Bank Int'l, 134 S. Ct. 2347 (2014), and Mayo Collaborative Servs. v. Prometheus Laboratories, Inc., 566 U.S. 66 (2012). Following the methodology of Alice and Mayo, the court first concluded that the method in the claims was directed to a natural law—namely, that "the presence of MPO in a bodily sample is correlated to its relationship to [CVD]"—because "the method starts and ends with naturally occurring phenomena with no meaningful non-routine steps in between[.]" Id. at 1361. Next, the court found that the "claims, whether considered limitation-by-limitation or as a whole, do not sufficiently transform the natural existence of MPO in a bodily sample and its correlation to cardiovascular risk into a patentable invention." Id. at 1362. Accordingly, it affirmed the district court's finding that the '552 patent and its companion patents were invalid. Id. at 1364.[6]

II. DISCUSSION

A. Standard of Review

The Fourth Circuit has recognized three grounds for reconsideration under Fed. R. Civ. P. 59: "(1) an intervening change in the controlling law, (2) new evidence that was not available at trial, or (3) that there has been a clear error of law or a manifest injustice," Robinson v. Wix Filtration Corp., LLC, 599 F.3d 403, 407 (4th Cir. 2010). Because the Federal Circuit's published opinion in Cleveland Clinic I provides significant clarification regarding the controlling law that was not available when the Court initially considered defendant's Motion to Dismiss, reconsideration is appropriate.

According to Fed. R. Civ. P. 12(b)(6), a complaint should be dismissed if it fails to state a claim upon which relief can be granted. "To survive a motion to dismiss, a complaint must set

[6] During oral argument, plaintiffs' counsel indicated that they were considering a petition for rehearing, although counsel has conceded that the likelihood of the Federal Circuit granting the petition was not promising given that the panel's decision was unanimous.

forth sufficient factual matter, accepted as true, to 'state a claim for relief that is plausible on its face.'" Ashcroft v. Iqbal, 556 U.S. 662, 678 (2009) (quoting Bell Atlantic Corp. v. Twombly, 550 U.S. 544, 547 (2007)). The Court must "assume that the facts alleged in the complaint are true and draw all reasonable inferences in the plaintiff's favor," Burbach Broad. Co. of Del. v. Elkins Radio Corp., 278 F.3d 401, 406 (4th Cir. 2002), but only to the extent that those allegations pertain to facts rather than to legal conclusions, Iqbal, 556 U.S. at 678.

Plaintiffs maintain, as they did in Cleveland Clinic I, that considering the patentability of a claimed invention on a Rule 12(b)(6) motion is inappropriate, particularly in complex life sciences cases. In Cleveland Clinic I, the Federal Circuit was unmoved by that argument, emphasizing that it has "repeatedly affirmed § 101 rejections at the motion to dismiss stage, before claim construction or significant discovery has commenced." Cleveland Clinic I, 859 F.3d at 1360. The key question is whether discovery is required for "a full understanding of the basic character of the claimed subject matter." Bancorp Servs., LLC v. Sun Life Assurance Co. of Canada (U.S.), 687 F.3d 1266, 1273–74 (Fed. Cir. 2012). When a party has "provided no proposed construction of any terms or proposed expert testimony that would change the § 101 analysis," there is no reason to postpone the eligibility decision until discovery can take place. See Cleveland Clinic I, 859 F.3d at 1360.

Finally, plaintiffs argue that § 101 challenges to patents issued after Alice and Mayo, such as the '065 and '567 patents, are subject to a higher standard of proof than challenges to patents issued before those decisions. Pl. Opp., [Dkt. 68] at 3. This argument fails because a party challenging the validity of any patent must establish invalidity by clear and convincing evidence, see Microsoft Corp. v. I4I Ltd. P'ship, 564 U.S. 91, 111–114 (2011), and no court has held that a higher standard of proof applies for patents issued after Alice and Mayo.

See Cadence Pharm. Inc. v. Exela PharmSci Inc., 780 F.3d 1364, 1375 (Fed. Cir. 2015) (applying the clear and convincing standard); see also SkillSurvey, Inc. v. Checkster LLC, 178 F. Supp. 247, 255 (E.D. Pa. 2016) ("The standard is not clear and convincing for pre-Alice patents, but clearer and more convincing for post-Alice patents.").

B. Section 101 Patentability ('065 and '597 Patents)

1. Differences from Invalidated Parent Patent

Plaintiffs argue that the Federal Circuit's opinion in Cleveland Clinic I does not control the outcome of this civil action because the patents at issue here are different from those at issue in the Ohio case. Although there are some differences among the various patents, they are not sufficiently distinct to render the Federal Circuit's decision irrelevant to the patents at issue.

The representative claims in the parent '552 patent at issue in Cleveland Clinic I recited "a method for assessing a test subject's risk of having" CVD consisting of "comparing" the MPO levels in samples taken from a patient to MPO levels in samples from control subjects known not to have the disease and determining whether the patient's levels were "elevated." Cleveland Clinic I, 859 F.3d at 1356. Plaintiff correctly argues that the first difference between the patents at issue here and those invalidated in Cleveland Clinic I is that they begin with a patient already known to have atherosclerotic CVD. Accordingly, the methods claimed in the '065 and '597 patents are not primarily aimed at diagnosing whether the test subject is suffering from CVD. Instead, they are described, respectively, as a "method of detecting elevated MPO mass in a patient sample," [Dkt. 35-1] at C0000332, and a "method for identifying an elevated [MPO] concentration in a plasma sample from a human subject with atherosclerotic" CVD, [Dkt. 35-2] at C0000659. Plaintiffs refer to patents featuring claims akin to those in the '552 patent as

"diagnostic patents," contrasting them with patents such as the '065 and '597 patents, which they term "laboratory method patents."

Additionally, plaintiffs point to several steps in the claims in the '065 and '597 patents that were not explicitly included in the Cleveland Clinic I patents. Specifically, where the '552 patent simply taught "determining" the level of MPO mass or activity from blood or its byproducts (or treated the MPO level as a given), the '065 patent teaches that the MPO mass level be detected "by contacting said plasma sample with anti-MPO antibodies and detecting binding between MPO in said plasma sample and said anti-MPO antibodies." Compare Cleveland Clinic I, 859 F.3d at 1356, with [Dkt. 35-1] at C0000332. The process claimed in the '597 patent is even more detailed, requiring "contacting a sample [of human plasma from a subject with atherosclerotic CVD] with an anti-MPO antibody;" "spectrophotometrically detecting MPO levels in said plasma sample;" "comparing said MPO levels in said plasma sample to a standard curve generated with known amounts of MPO to determine the MPO concentration in said sample;" and "comparing" the MPO concentration to a control sample to "identify" it as elevated. [Dkt. 35-2] at C0000659.[7] None of these additional steps explicitly appeared in the Cleveland Clinic I patents' claim language, and because the question of eligibility under § 101 turns on whether those steps are "conventional," see infra, this Court must conduct an additional § 101 analysis incorporating those steps despite Cleveland Clinic I having affirmed the '552 patent's invalidity.

[7] Claim 2 in the '597 patent teaches the same method, preceded by using a centrifuge to obtain the plasma sample from "an anti-coagulated blood sample[.]"

2. Patentability of the '065 and '597 Patents

Section 101 of the Patent Act makes "any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof" eligible for patent protection. 35 U.S.C. § 101. Despite its breadth, the Supreme Court "has long held that this provision contains an important implicit exception: '[L]aws of nature, natural phenomena, and abstract ideas' are not patentable." Mayo, 566 U.S. at 70 (quoting Diamond v. Diehr, 450 U.S. 175, 185 (1981)) (alteration in original). "Such discoveries are manifestations of nature, free to all men and reserved exclusively to none." Id. (internal quotation omitted). Although "too broad an interpretation of this exclusionary principle could eviscerate patent law" because "all inventions at some level embody, use, . . . or apply laws of nature," id., "to transform an unpatentable law of nature into a patent-eligible application of such a law, one must do more than simply state the law of nature while adding the words 'apply it,'" id. at 72 (emphasis in original).

The Supreme Court has adopted a two-step "framework for distinguishing patents that claim laws of nature . . . from applications of those concepts." Ariosa Diagnostics, Inc. v. Sequenom, Inc., 788 F.3d 1371, 1375 (Fed. Cir. 2015), reh'g denied, 809 F.3d 1282 (Fed. Cir. 2015), cert. denied 136 S. Ct. 2511 (2016). In the first step, courts "determine whether the claims at issue are directed to a patent-ineligible concept." Id. "If the answer is yes, then [courts] next consider the elements of each claim both individually and 'as an ordered combination' to determine whether additional elements 'transform the nature of the claim' into a patent-eligible application." Id. (quoting Mayo, 566 U.S. at 78–79). This second step involves "a search for an 'inventive concept'—i.e., an element or combination of elements that is 'sufficient to ensure that the patent in practice amounts to significantly more than a patent upon

the [ineligible concept] itself.'" Id. (quoting Mayo, 566 U.S. at 72–73 (alteration in original)). At step two, "well-understood, routine, conventional activity previously engaged in by scientists who work in the field . . . . is normally not sufficient to transform an ineligible law of nature into a patent-eligible application of such a law." Mayo, 566 U.S. at 79.

At the outset, there can be no dispute that the correlation between elevated MPO and CVD is a natural law given that the Federal Circuit explicitly found as much in Cleveland Clinic I. 859 F.3d at 1361–63. Accordingly, the issue before this Court is whether the '065 and '597 patents are directed to that natural law. Plaintiffs' argument that these patents are not directed to a law of nature relies on the reasoning of the patent examiners, who found the analogy to USPTO Guidelines Example 29, Claim 1 persuasive.[8] In that example, the patent merely claims "a method for detecting [the protein] JUL-1," in contrast to the latter two claims, which claim a "method for diagnosing [the fictional disease] julitis." Under the USPTO's reasoning, the first example is not directed to an ineligible natural law because all it claims is the method for detecting the relevant protein, rather than correlating the protein with the disease. [Dkt. 35-7] at 15. It is that correlation which constitutes a law of nature. According to plaintiffs, the same is true here: because the '065 and '597 patents merely claim a laboratory method of "detecting" MPO activity, as opposed to a diagnostic method, they are not directed to patent ineligible subject matter. Pl. Memo., [Dkt. 46] at 16.

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[8] Plaintiffs argue that these guidelines are entitled to Skidmore deference. That is wrong because there is no indication that these guidelines were adopted through the kind of process that warrants such deference, "for example, formal adjudication or notice and comment rulemaking." See Christensen v. Harris County, 529 U.S. 576, 587 (2000) (plurality op.). Although the Federal Circuit has cited these guidelines in the past, notably the court did not hold that they were entitled to deference, only that they were accurate and persuasive on the facts of the instant case. See Carnegie Mellon Univ. v. Hoffmann-La Roche Inc., 541 F.3d 1115, 1124 (Fed. Cir. 2008). For the reasons that follow, the Court finds that the examiner's application of Example 29 in this instance is neither accurate nor persuasive.

Plaintiffs' argument is overly superficial. Although laboratory methods may be more likely to survive a § 101 inquiry, see Cleveland Clinic I, 859 F.3d at 1361, their survival is not automatic. As defendant has aptly observed, the claims here contain qualifying language that distinguishes them from Example 29, Claim 1 and reveals that they remain directed to the natural law—that is, the correlation of CVD to elevated MPO—rather than the laboratory method itself. In particular, unlike the guidelines example, which was directed simply to a "method of detecting JUL-1," the claims in the '065 patent are directed to a "method of detecting elevated MPO mass in a patient sample . . . from a human patient having atherosclerotic [CVD]," and the claims in the '597 patent are directed to a "method for identifying an elevated [MPO] concentration in a plasma sample from a human subject with atherosclerotic CVD" (emphases added). Given this language, the method is therefore only useful for detecting the elevated level of MPO linked to CVD—that is, for detecting the natural phenomenon. It is not a general laboratory technique for detecting MPO levels. Because the method is directed at detecting the correlation that is the natural law, rather than MPO levels generally, it is clear that the method is directed to the natural law. See Cleveland Clinic I, 859 F.3d at 1361 ([T]he method starts and ends with naturally occurring phenomena with no meaningful non-routine steps in between . . . . The claims are therefore directed to a natural law."). Accepting plaintiffs' argument to the contrary would permit artful drafters to recast any diagnostic patent as a laboratory method patent, frustrating the purpose of the natural law exception. Accordingly, the USPTO's reliance on Example 29 was misplaced, and these claims are directed to the natural law that persons with CVD have higher levels of MPO.

Even if a patent is directed to a natural law, under Mayo the Court must determine whether the additional steps in the claimed methods are a sufficiently "inventive concept" to

render the claims patent eligible. Mayo, 566 U.S. at 72, 79–80. Considered independently and as an ordered combination, the additional steps in both the '065 and '597 patents are insufficiently inventive to save the claims.

Beginning by considering the steps independently, the '065 patent only consists of three steps: "obtaining a plasma sample," "detecting . . . MPO mass . . . by contacting said plasma sample with anti-MPO antibodies and detecting binding;" and comparing the MPO level of the sample to "a control MPO mass level from the general population or apparently healthy subjects[.]" [Dkt. 35-1] at C0000332. Each of these steps is conventional. Little argument could be made regarding the first and third steps—obtaining a plasma sample and comparing one MPO level to a healthy level are quotidian medical tasks. See Cleveland Clinic I, 859 F.3d at 1362 ("Cleveland Clinic does not purport to derive new statistical methods to arrive at the predetermined or control levels of MPO . . . . Known statistical models can be employed[.]"); PerkinElmer, Inc. v. Intema Ltd., 496 F. App'x 65, 72 (Fed. Cir. 2012) (holding that a comparison step is "an ineligible mental step" when the control sample was naturally occurring). In Cleveland Clinic I, the Federal Circuit also rejected the notion that, step two, using antibodies to detect MPO in the blood was unconventional when it concluded that the dependent claims in the '552 patent, which included an "immunological technique" for detecting MPO, "merely recite[d] known methods of detecting MPO[.]"[9] 859 F.3d at 1360 (citing the '552 Patent, [Dkt.

[9] The specification makes it clear that an "immunological technique" is one in which the sample is contacted with antibodies. See '552 Specification, [Dkt. 64-2] at 42 ("The mass of [MPO] in a given sample is readily determined by an immunological method, e.g. ELISA."); id. at 49 ("MPO mass per neutrophil was determined using an enzyme linked immunosorbent assay (ELISA). Capture plates were made by incubating 96-well plates with polyclonal antibody . . . raised against the heavy chaining of human MPO . . . . Plates were washed and sandwich ELISA performed . . . using alkaline phosphatase-labeled antibody to human MPO. MPO mass was calculated based on standard curves generated with known amounts of human MPO[.]")

64-2] at 52–53). Similarly, the patent examiner, whose findings plaintiffs rely on, concluded that "it was well known in the art to detect MPO levels using antibodies directed against MPO." [Dkt. 35-5] at 37. Even the specifications of the '065 and '597 patents concede that MPO activity "may be determined by any of a variety of standard methods known in the art." [Dkt. 35-1] at C0000321; [Dkt. 35-2] at C0000648 (emphasis added). Accordingly, each of the added steps in the '065 patent is "well-understood, routine, conventional activity previously engaged in by scientists who work in the field." Mayo, 566 U.S. at 73.[10]

The steps added in the '597 patent, considered independently, also offer plaintiffs no assistance. Two steps, contacting the MPO sample with an antibody and comparing MPO concentration to a control sample, repeat steps in the '065 patent, and are conventional for the reasons already stated. Similarly, plaintiffs have not challenged the patent examiner's findings that, looking at these steps independently, "spectrophotometrically detecting MPO levels was known," [Dkt. 35-10] at 70, and "standard curves using MPO were used in the art," [Dkt. 35-9] at 36. Claim 2 repeats these steps, adding that plasma is obtained by "centrifuging an anti-coagulated blood sample[.]" [Dkt. 35-2] at C0000659. Once again, plaintiffs have not challenged the examiner's finding that the prior art taught "obtaining blood samples from an anticoagulation . . . followed by isolation of the plasma by centrifugation." [Dkt. 35-9] at 36. Consequently, none of the steps in the '597 patent are novel.

Plaintiffs' strongest argument is that the ordered combination of steps recited in these claims has not been previously used for this particular purpose. As plaintiffs have stated it, "it is

[10] Plaintiffs have also argued that their methods were inventive as compared to specific examples of prior art, including using a C-reactive protein to predict the risk of heart attack and using commercially available kits to detect MPO. Regardless of whether plaintiffs' methods differ from those particular techniques, they are not inventive when compared to the entire corpus of prior art for the reasons described above.

not well-understood, routine, or conventional to detect elevated MPO levels in plasma from a subject having atherosclerotic CVD." Pl. Memo., [Dkt. 46] at 19 (internal quotation omitted) (emphases in original). As they did in Cleveland Clinic I, plaintiffs analogize to Rapid Litigation Management Ltd. v. CellzDirect, Inc., 827 F.3d 1042 (Fed. Cir. 2016), arguing that this particular use of the steps "goes against 'prevailing wisdom.'" Id. at 20 (quoting CellzDirect, 827 F.3d at 1051).

The analogy to CellzDirect is inapt. See Cleveland Clinic I, 859 F.3d at 1362 (rejecting the same analogy). In CellzDirect, the inventors discovered that certain liver cells could survive multiple cycles of being frozen and thawed. 827 F.3d at 1045. Applying this discovery, the inventors claimed an improved process for preserving those cells by freezing them more than once and separating out the cells that were unable to survive this process between the freezings. Id. The Federal Circuit concluded that "[r]epeating a step that the art taught should be performed only once can hardly be considered routine or conventional . . . . even though it was the inventor's discovery of something natural that led them to do so." Id. at 1051. Crucially, the court distinguished Ariosa by observing that the "end result of the . . . claims [was] not simply an observation or detection of" the natural law in question. Id. at 1048.

Like Ariosa, and unlike CellzDirect, the "end result" of the claims in the '065 and '597 patents is the "observation or detection" of the natural law. Id. This conclusion is supported by the claim language, which describes the methods, respectively, as designed to "detect" or "identify" "elevated MPO" activity in CVD patients. That CVD patients have higher MPO levels is the natural law in question. Cleveland Clinic I, 859 F.3d at 1362. Accordingly, the end result of these claims is "detecting" or "identifying" the natural law. See id. (concluding that the '552 patent "merely tell[s] those interested in the subject about the correlations that the

researchers discovered" (internal quotation omitted)). Plaintiffs have offered no other use for these methods. If merely using existing, conventional methods to observe a newly discovered natural phenomenon were enough to qualify for protection under § 101, the natural law exception would be eviscerated.

Plaintiffs also rely on Viveve, Inc. v. Thermigen, LLC, No. 2:16-cv-1189, 2017 WL 1425606 (E.D. Tex. Apr. 20, 2017), but that case only reinforces the conclusion that the '065 and '597 patents are directed to a patent-ineligible law of nature. The Viveve patent claimed "a method for remodeling a therapeutic zone within a target tissue [underlying an epithelium of female genital tissue][.]" Id. at *1. The court held that the patent "claim[ed] the application and synthetization of a natural law [i.e., that heat denatures collagen] into a concrete process, which builds upon the subject matter's capability of undergoing the process." Id. at *5. In reaching that conclusion, the court recognized that the patent stood "in stark contrast to those patents which the Federal Circuit has invalidated as directed to a natural law," which "typically encompass[ed] the pure observation or identification of the natural law at issue." Id. Here, unlike in Viveve, plaintiffs' methods are directed to "pure observation or identification of the natural law at issue"—that CVD generates higher MPO levels—and offer no additional inventive concept. Viveve therefore confirms the conclusion that the '065 and '597 patents are invalid.

Just as a patent must do more than simply "state the law of nature while adding the words 'apply it'" to claim eligible subject matter, Mayo, 566 U.S. at 72, it must do more than simply state the law of nature while adding the words "observe it." The plaintiffs here have not done so. Unlike the patents in CellzDirect and Viveve, the ordered combination of steps in the '065 and '597 patents does no more than observe the unpatentable natural phenomenon. Plaintiffs have not claimed any additional applied use of the claimed methods, meaning the patents teach no

more than observing the law of nature using "well-understood, routine, conventional activity previously engaged in by researchers in the field." Mayo, 566 U.S. at 73. As such, their claims are directed to subject matter that is ineligible for protection under § 101.

III. CONCLUSION

By all accounts, the plaintiffs have advanced the diagnosis of CVD with the methods described in these patents; however, under present law even what appears to be a "[g]roundbreaking, innovative, or even brilliant discovery does not by itself satisfy the § 101 inquiry." Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 133 S. Ct. 2107, 2117 (2013). Under existing precedent, this Court is bound to conclude that the claims in the '065 and '597 patents are not eligible for protection.

For these reasons, defendant's Motion to Reconsider will be granted and Counts 1 and 2 will be dismissed by an appropriate order to be issued with this Memorandum Opinion.

Entered this 4th day of August, 2017.

Alexandria, Virginia

/s/
Leonie M. Brinkema
United States District Judge